Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Ibalizumab (IBA, Trogarzo) (Last updated April 16, 2019; last reviewed April 16, 2019)

For additional information, see Drugs@FDA: http://www.accessdata.fda.gov/scripts/cder/daf

Formulations

Single-Dose Vial for Intravenous Administration: 200 mg/1.33 mL (150 mg/mL) in a single-dose vial

Dosing Recommendations

Child and Adolescent Dose:

- The safety and efficacy of using ibalizumab in children and adolescents has not been established.

Adult Dose:

- A single loading dose infusion of 2,000 mg administered intravenously (IV) over 30 minutes is followed by a maintenance dose of 800 mg administered IV over 15 minutes every 2 weeks.
- Food and Drug Administration approval is limited to heavily treatment-experienced adults with multidrug-resistant HIV infection who are experiencing treatment failure on their current regimen.
- Ibalizumab is used in combination with other antiretroviral drugs.

Selected Adverse Events

- Diarrhea, dizziness, nausea, rash
- Immune reconstitution inflammatory syndrome
- Potential for immunogenicity in the form of anti-ibalizumab antibodies

Special Instructions

- Using aseptic technique, withdraw 1.33 mL from each vial and transfer into a 250 mL bag of 0.9% sodium chloride for IV injection. Other IV diluents must not be used.
- Once diluted, the solution should be administered immediately. If not used immediately, the solution can be stored at room temperature for up to 4 hours or refrigerated for up to 24 hours. Refrigerated solution should be allowed to stand at room temperature for at least 30 minutes but no more than 4 hours prior to administration.
- Diluted solution is administered as an IV infusion, not as a bolus or IV push.

Metabolism/Elimination

- Monoclonal antibodies are metabolized to peptides and amino acids

Drug Interactions (see also the Adult and Adolescent Antiretroviral Guidelines and HIV Drug Interaction Checker)

Ibalizumab is a humanized IgG4 monoclonal antibody that blocks HIV entry into CD4 T lymphocytes (CD4). Based on ibalizumab's mechanism of action and target-mediated drug disposition, drug-drug interactions are not expected. However, no drug interaction studies have been conducted.[1]

Major Toxicities

- *More common:* Rash, diarrhea, headache, nausea, dizziness, and depression.[1,2]
- *Less common (more severe):* Immune reconstitution inflammatory syndrome.[1]

Resistance

Ibalizumab resistance mutations will be cataloged on the following websites, which are routinely updated with new findings: the International Antiviral Society-USA (IAS-USA) list of updated resistance mutations

and the Stanford University HIV Drug Resistance Database.

Reduced susceptibility to ibalizumab, as defined by a decrease in maximum percent inhibition, occurs when HIV loses N-linked glycosylation sites in the V5 loop of glycoprotein 120.[1,2]

Phenotypic and genotypic test results showed no evidence of cross resistance between ibalizumab and any approved classes of antiretroviral (ARV) drugs.[3] Ibalizumab exhibits ARV activity against R5-tropic, X4-tropic, and dual-tropic HIV.[3]

Pediatric Use

Approval

Ibalizumab is not approved for use in pediatric patients. Ibalizumab was approved by the Food and Drug Administration in 2018 for use in adults in combination with other ARV drugs, with approval limited to heavily treatment-experienced adults with multidrug-resistant HIV who are experiencing treatment failure on their current regimen.[4]

Efficacy in Clinical Trials

Trial TMB-301 was conducted in 40 adults who were 23 to 65 years old, who had body weights ranging from 50 kg to 130 kg, who had resistance to ARV drugs from three classes, who had been treated for at least 6 months on stable ARV regimens and had viral loads >1,000 copies/mL, and who had viral sensitivity to at least one ARV drug.[4,5] Participants continued their current ARV regimens and received a 2,000-mg loading dose of ibalizumab on Day 7 of the study. One week after the loading dose, participants optimized their ART regimens. Participants received ibalizumab 800 mg on Day 21 and every 2 weeks thereafter. At Week 25, 43% of participants achieved suppressed viral loads of <50 copies/mL.[1,5] At Week 48 of an open-label extension study, 24 participants were taking ibalizumab and their optimized ARV regimen. Fifty nine percent of participants (16 of 27 participants) had viral loads <50 copies/mL at 48 weeks.[6,7]

Formulation and Mechanism of Action

Ibalizumab is a recombinant humanized monoclonal antibody that blocks HIV from infecting CD4 cells by binding to domain 2 of the CD4 receptor and interfering with post-attachment steps required for the entry of HIV virus particles into host cells and preventing the viral transmission that occurs via cell-cell fusion.[1,7] Since ibalizumab binds to a conformational epitope located primarily in domain 2 of the extracellular portion of the CD4 receptor, away from Major Histocompatibility Complex II molecule binding sites, it does not interfere with CD4-mediated immune functions.

Ibalizumab is formulated in single-dose vials. The solution in the vial has to be diluted in 0.9% Sodium Chloride Injection and administered by intravenous infusion. Inactive ingredients include L-histidine, polysorbate 80, sodium chloride, and sucrose.

References

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